

TOWNSEND and TOWNSEND and CREW LLP

By: Lillian M. Montano

PATENT

Attorney Docket No.: 022266-000930US
Client Reference No.: ORMF Ref. No.
1999-009-001; UIC Ref. No. BTUL
CT34/NPU-1(A)/DIV/CON.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Gerald Koelsch, et al.

Application No.: 10/773,754

Filed: February 6, 2004

For: INHIBITORS OF MEMAPSIN 2
AND USE THEREOF

Confirmation No.: 5585

Examiner: Suzanne Marie Noakes

Art Unit: 1653

**INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The references cited on attached form PTO/SB/08B are being called to the attention of the Examiner. This application is a continuation of and relies on U.S. Patent Application No. 09/845,226, filed April 30, 2001 (Attorney Docket No. 022266-000920US), which is a divisional of and relies on U.S. Patent Application No. 09/603,713, filed June 27, 2000 (Attorney Docket No. 022266-000910US) for an earlier effective filing date under 37 U.S.C. §120. In accordance with 37 CFR §1.98(d), copies of those references that have been previously submitted to or cited by the Patent Office in the parent applications are not enclosed. Copies of references FK-FL have not been previously cited, and are therefore enclosed.

Further, Applicants attach a copy of an Australian Examination Report dated June 26, 2006, which was issued in counterpart Australian application No. 2004202058, and in which references FK-FL were cited.

TP

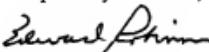
It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

This IDS is being filed before the mailing date of the final Office Action or Notice of Allowance.

Please charge the IDS fee of \$180 to Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



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Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	3	of	11	Attorney Docket Number	022268-000940US
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U.S. PATENT DOCUMENTS+

Examiner Initials*	Cite No. ²	Document Number Number Kind Code ³ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Column, Line, Where Relevant Passages or Relevant Figures Appear
AA	US-4,923,967		05/08/90	Bobbitt, et al	
AB	US-5,221,607		06/22/93	Cordel, et al	
AC	US-5,252,463		10/12/93	Nelson, et al	
AD	US-5,235,043		06/10/93	Collins, et al	
AE	US-5,744,346		04/28/98	Chrysler, et al	
AF	US-6,207,710 B1		03/27/01	Aude, et al	
AG	US-6,245,884 B1		06/12/01	Hock	
AH	US-6,281,223 B1		09/16/01	Christe, et al	
AI	US-6,313,266 B1		11/06/01	Hock	
AJ	US-6,319,889 B1		11/20/01	Powell, et al	
AK	US-6,328,163 B1		12/11/01	Anderson, et al	
AL	US-6,361,975 B1		03/28/02	Chrase, et al	
AM	US-6,420,534 B1		07/16/02	Gumey, et al	
AN	US-6,545,127		04/06/03	Teng, et al	
AO	US-2002/0091834 A1		07/16/02	Gumey, et al	
AP	US-2002/0055459 A1		05/09/02	Chopre, et al	
AQ	US-2002/0072050 A1		08/13/02	Hock	
AR	US-2002/0037315 A1		03/26/02	Gumey, et al	
AS	US-2002/0159991 A1		10/31/02	Cordel, et al	
AT	US-2002/0157122 A1		10/24/02	Wong, et al	
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FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ²	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Column, Line, Where Relevant Passages or Relevant Figures Appear	T ⁴
		Country Code ³	Number ⁴ Kind Code ⁵ (if known)				
AV	WO 96/40885	WO	A2	12/19/96			
AW	WO 97/27296	WO	A1	07/31/97			
AX	WO 98/13488	WO	A2	04/02/98			
AY	WO 98/15828	WO	A1	04/16/98			
AZ	WO 98/21569	WO	A1	05/22/98			
BA	WO 98/26059	WO	A1	05/18/98			
BB	WO 98/51752	WO	A1	10/14/98			
BC	WO 98/64567	WO	A1	12/16/98			
BD	WO 00/17368	WO	A3	03/30/00			
BE	WO 00/23576	WO	A3	04/27/00			
BF	WO 00/47618	WO	A2	08/17/00			
BG	WO 00/56479	WO	A1	10/05/00			
BH	WO 00/77030	WO	A1	12/21/00			

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²Applicant's unique citation designation number (optional). ³Applicant is to place a check mark here if English language Translation is attached.

Substitute for form 1449B/PTO				Complete If Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT					
(use as many sheets as necessary)					
Sheet	4	of	11		
Attorney Docket Number 022286-000940US					

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ²
		Country Code ³	Number ⁴				
BI	WO	01/23533	A2	04/05/01			<input type="checkbox"/>
BJ	WO	01/70672	A1	09/27/01			<input type="checkbox"/>
BK	WO	02/47466	A2	06/20/02			<input type="checkbox"/>
BL	WO	02/25276	A1	03/28/02			<input type="checkbox"/>
BM	EP	0855444	A2	07/29/88			<input type="checkbox"/>
BN	EP	0302469	A2	02/06/89			<input type="checkbox"/>
BO	JP	10108681	A	04/28/88			<input type="checkbox"/>

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Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/820,953
(use as many sheets as necessary)				Filing Date	April 4, 2004
				First Named Inventor	Jordan J.N. Tang
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet 5		of 11	Attorney Docket Number 022266-000940US		

NON PATENT LITERATURE DOCUMENTS						T ²
Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published				T ²
	BP	ABAD-ZAPATERO et al., "Structure of a secreted aspartic protease from <i>C. albicans</i> complexed with a potent inhibitor: implications for the design of antifungal agents," <i>Protein Sci</i> 5(4):640-52 (1996).				
	BQ	ABBENATE, et al., "Inhibitors of β -amyloid formation based on the β -secretase cleavage site," <i>Biochemical and Biophysical Research Communications</i> 268(1):133-136 (2000).				
	BR	ASKEW, et al., "Molecular recognition with convergent functional groups. Synthetic and structure studies with a model receptor for nucleic acid components," <i>J Am Chem Soc</i> 111:1082-1080 (1989).				
	BS	ADAMS, M.D., et al., JP10106861/14Cathespin K Gene Instruct - MicroPatent Bibliographic Database [Online]. Retrieved from the Internet - URL: http://www.micropat.com/htdocs/com...micro.00587727/JP/JP10106861.html				
	BT	BAILEY & COOPER, "A structural comparison of 21 inhibitor complexes of the aspartic proteinase from <i>Endothia parasitica</i> ," <i>Protein Sci</i> 3(11):2129-43 (1994).				
	BU	BRUNGER, et al., "Crystallography & NMR system: A new software suite for macromolecular structure determination," <i>Acta Crystalogr D Biol Crystalogr</i> 64 (Pt 8):905-21 (1998).				
	BV	CAPELLI, et al., "The proteolytic fragments of the Alzheimer's disease-associated presenilin-1 form heterodimers and occur as a 105-150-kDa molecular mass complex," <i>J Biol Chem</i> 273(6):3205-11 (1998).				
	BW	CHARTIER-HARLIN, et al., "Early-onset Alzheimer's disease caused by mutations at codon 717 of the beta-amyloid precursor protein gene," <i>Nature</i> 353(6347):544-5 (1991).				
	BX	CITRON, et al., "Mutation of the beta-amyloid precursor protein in familial Alzheimer's disease increases beta-protein production," <i>Nature</i> 360(6426):672-4 (1992).				
	BY	COHEN, et al., "An artificial cell-cycle inhibitor isolated from a combinatorial library," <i>Proc Natl Acad Sci USA</i> 95(24):14272-7 (1998).				
	BZ	CORDIER, et al., "Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's DISEASE in late onset families," <i>Science</i> 281(5123):921-3 (1998).				
	CA	COWLEY, et al., "Alzheimer's unlocking the mystery," <i>Newsweek</i> January 31, 2000.				
	CB	CUTFIELD, et al., "The crystal structure of a major secreted aspartic proteinase from <i>Candida albicans</i> in complexes with two inhibitors," <i>Structure</i> 3(11):1281-71 (1995).				
	CC	DAVIES, "The structure and function of the aspartic proteinases," <i>Annu Rev Biophys Chem</i> 9:189-215 (1990).				
	CD	DEALWIS, et al., "X-ray analysis at 2.0 Å resolution of mouse submaxillary renin complexed with a decapeptide inhibitor CH-56, based on the 4-16 fragment of rat angiotensinogen," <i>J Mol Biol</i> 236(1):342-50 (1994).				
	CE	DE STROOPER, et al., "Deficiency of presenilin-1 inhibits the normal cleavage of amyloid precursor protein," <i>Nature</i> 391(6665):387-90 (1998).				

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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/820,953
(use as many sheets as necessary)				Filing Date	April 4, 2004
Sheet	6	of	11	First Named Inventor	Jordan J.N. Tang
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
				Attorney Docket Number	022286-000940US

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T ²
	CF	DORRELL, S "Unraveling Alzheimer's Disease with β -secretase Inhibitors," <i>Drug Discovery Today</i> , 5(8):316-317 (2000).			
	CG	DUNN, Structure and Functions of the Aspartic Proteinases, <i>Adv. In Exptl. Med. Biol.</i> 306 (Plenum Press, NY 1991)			
	CH	ELLINGTON & SZOSTAK, "In vitro selection of RNA molecules that bind specific ligands," <i>Nature</i> 346(6287) 818-22 (1990).			
	CI	ERMOLIEFF et al., "Proteolytic activation of recombinant Pro-memapsin 2 (Pro- β -secretase) studied, with new fluorogenic substrates," <i>Biochemistry</i> 39(40):12450-12458 (2000).			
	CJ	EZZELL, C. "Alzheimer's Alchemy," <i>Science News</i> (1992) 141:152-153			
	CK	FAN, et al., "BACE Maps to chromosome 11 and a BACE homolog, BACQ2, resides in the cbl/gata down syndrome region of chromosome 21," <i>Science</i> 285:1255a (1999).			
	CL	FIELDS & SONG, "A novel genetic system to detect protein-protein interactions," <i>Nature</i> 340(6230):248-8 (1999).			
	CM	GHOSH & FIDANZI, Transition-state mimetics for HIV protease inhibitors: Sterecontrolled synthesis of hydroxymethylene and hydroxymethylidene isosteres by ester-derived titanium enolate syn and anti-aldol reactions," <i>Org. Chem.</i> 63(9):148-54 (1998).			
	CN	GHOSH, A.K. et al., "Structure-Based Design: Potent Inhibitors of Human Brain Memapsin 2 (β -Secretase)," <i>J. Med. Chem.</i> 44:2855-2868 (2001).			
	CO	GHOSH et al., "Design of potent inhibitors for human brain memapsin 2 (β -secretase)," <i>J. Am Chem Soc</i> 122(14):3622-3623 (2000).			
	CP	GLENNIER & WONG, "Alzheimer's disease: Initial report of the purification and characterization of a novel cerebrovascular amyloid protein," <i>Biochem Biophys Res Commun</i> 120(3):885-90 (1984)			
	CQ	GOATE, et al., "Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease," <i>Nature</i> 349(6211):704-6 (1991).			
	CR	GOLDGABER, et al., "Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease," <i>Science</i> 235(4791):677-80 (1987).			
	CS	GURNEY, M. E. et al., "U.S. Published Patent Application, US 2002/0037315 A1," published Mar. 28, 2002, filing date Feb. 27, 2001.			
	CT	HAASS & DE STROOPER, "The presenilins in Alzheimer's disease—Proteolysis holds the key," <i>Science</i> 286:916-918 (1999).			
	CU	HONG et al., "Structure of the protease domain of memapsin 2 (β -secretase) complexed with inhibitor," <i>Science</i> 280:150-153 (2000).			

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				First Named Inventor	Jordan J.N. Tang
				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
Sheet	7	of	11	Attorney Docket Number	022288-000940US

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T *
	CV	HOWLETT, D.R. et al., "In search of an enzyme: the β -secretase of Alzheimer's disease is an aspartic proteinase," <i>Trends Neurosci</i> 23:565-570 (2000).			
	CW	JAMES, Aspartic Proteinases, Retroviral and Cellular Enzymes, <i>Adv. in Exptl. Med. Biol.</i> 438 (Plenum Press, NY 1995).			
	CX	JONES, et al., "Improved methods for binding protein models in electron density maps and the location of errors in these models" <i>Acta Crystlogr A</i> 47 (Pt 2):110-9 (1991).			
	CY	JORM, ed., <i>A Guide to the Understanding of Alzheimer's Disease and Related Disorders</i> (New York University Press, New York 1987).			
	CZ	KANG, et al., "The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor," <i>Nature</i> 325(6106):733-6 (1987).			
	DA	KEARNEY & AWEKA, "The penetration of anti-infectives into the central nervous system," <i>Neural. Clin.</i> 17(4):883-900 (1999).			
	DB	KELLY & DOW, "Microbial differentiation: the role of cellular asymmetry," <i>Microbiol Sci</i> 1:214-8 (1994).			
	DC	KHAN, et al., "Lowering the entropic barrier for binding conformationally flexible inhibitors to enzymes," <i>Biochemistry</i> 37(40):16639-45 (1998).			
	DD	KNOPP, et al., "Cell-type and amyloid precursor protein-type specific inhibition of A beta release by batrachotoxin A1, a selective inhibitor of vacuolar ATPases," <i>J Biol Chem</i> 276(6):2419-22 (1990).			
	DE	KOLATA, "Scientists find enzyme linked to Alzheimer's," <i>National Science/Health</i> October 22, 1999.			
	DF	KOSTKA, <i>Aspartic proteinases and Their Inhibitor</i> (Walter de Gruyter, Berlin 1983).			
	DG	LASKOWSKI, et al., "Procheck: a program to check the stereochemical quality of protein structures," <i>J Appl. Crystalogr</i> 26:253 (1993).			
	DH	LEMAIRE, et al., "The PreA4(95) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons," <i>Nucleic Acids Res</i> 17(2):817-22 (1989).			
	DI	LEVY et al., "Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type," <i>Science</i> 246(4949):1124-6 (1990).			
	DJ	LEVY-LAHAD, et al., "Candidate gene for the chromosome 1 familial Alzheimer's disease locus," <i>Science</i> 269(5228):973-7 (1995).			
	DK	LEWIS & DEAN, "Automated site-directed drug design: the concept of spacer skeletons for primary structure generation," <i>Proc R Soc Lond B Biol Sci</i> 238(1283):125-40 and 141-162 (1999).			

Examiner Signature		Date Considered
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Sheet	8	of	11	First Named Inventor	Jordan J.N. Tang
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NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *	Cite No. *	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			T *
	DL	LIN, et al., "Intracellular diversion of glycoprotein GPI-140 of human immunodeficiency virus to lysosomes as a strategy of AIDS gene therapy," <i>FASEB J</i> (11):1070-80 (1993).			
	DM	LIN et al., "Human aspartic protease memapsin 2 cleaves the β -secretase site of β -amyloid precursor protein," <i>PNAS</i> 97(4):1456-1460 (2000).			
	DN	MAJER, P. et al., "Structure-based subsite specificity mapping of human cathepsin D using statine-based inhibitors," <i>Protein Science</i> , 6(7):1458-1466 (1997).			
	DO	MANN, "Cerebral amyloidosis, ageing and Alzheimer's disease: a contribution from studies on Down's syndrome," <i>Neurology of Aging</i> 10(5):397-9 (1989).			
	DP	MARCINSZYN, et al., "Mode of inhibition of acid proteases by pepstatin," <i>J Biol Chem</i> 251(22):7088-94 (1976).			
	DQ	MARTSON, F.A.O. et al., "Solubilization of protein aggregates," <i>Methods of Enzymology</i> , 162:254-278 (1990).			
	DR	MATSUMOTO, et al., "Molecular cloning of human cDNA with a sequence highly similar to that of the dihydrofolate reductase gene in brain libraries derived from Alzheimer's patients," <i>Eur. J. Biochem</i> 232:337-343 (1993).			
	DS	MECKELEIN, et al., "Identification of a novel serine protease-like molecule in human brain," <i>Molecular Brain Research</i> 58:181-187 (*1998).			
	DT	MCKINLAY & ROSSMANN, "Rational design of antiviral agents," <i>Annu Rev Pharmacol Toxicol</i> 29:111-22 (1989).			
	DU	MULLAN, et al., "A locus for familial early-onset Alzheimer's disease on the long arm of chromosome 14, proximal to the alpha 1-antichymotrypsin gene," <i>Nat Genet</i> 2(4):340-2 (1992).			
	DV	MULLAN, et al., "A pathogenic mutation for probable Alzheimer's disease in the APP gene at the N-terminus of beta-amyloid," <i>Nat Genet</i> 1(6):345-7 (1992).			
	DW	MURRELL, et al., "A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease," <i>Science</i> 254(5028):97-9 (1991).			
	DX	NAVAZA, "AMoRe: an automated package for molecular replacement," <i>Acta Crystallogr Sect A</i> 50:157 (1997).			
	DY	DEFNER, C. et al., "Renin inhibition by substituted pipelines: A novel paradigm for the inhibition of monomeric aspartic proteinases?" <i>Chemistry & Biology (London)</i> , 8(3):127-131 (1999).			
	DZ	OTWINOWSKI & MINOR, "Processing of X-ray diffraction data collected in oscillation mode," <i>Methods Enzymol</i> 278:307 (1997).			
		PARIS, N. et al., "Bacterial Production and Purification of Recombinant Human Procalcitonin," <i>Biotechnology and Applied Biochemistry</i> , 12:438-440 (1990).			

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Sheet	9	of	11	Attorney Docket Number	022286-000940US

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	EA	PEREZ, et al., "Enhanced release of amyloid beta-protein from codon 67/671 "Swedish" mutant beta-amyloid precursor protein occurs in both secretory and endocytic pathways," <i>J Biol Chem</i> 271(18):9100-7 (1996)			
	EB	PERRY & DAVIES, <i>QSAR: Quantitative Structure-Activity Relationships in Drug Design</i> pp. 169-193 (Alan R. Liss, Inc. 1989)			
	EC	PHIMISTER, "Four companies announce discovery of b-secretase gene," <i>Nature Biotechnology</i> 18:18 (2000)			
	ED	POOLISHY, et al., "Presenilin proteins undergo heterogeneous endoproteolysis between Thr291 and A16299 and occur as stable N- and C-terminal fragments in normal and Alzheimer brain tissue," <i>Neurobiol Dis</i> 3(4):325-37 (1997)			
	EE	RIPKA, "Computers picture the perfect drug," <i>New Scientist</i> 54-57 (1986)			
	EF	ROBAKIS, et al., "Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides," <i>Proc Natl Acad Sci U S A</i> 84(12):4190-4 (1987)			
	EG	ROBERTS & SZOSTAK, "RNA-peptide fusions for the in vitro selection of peptides and proteins," <i>Proc Natl Acad Sci U S A</i> 94(23):12297-302 (1997)			
	EH	ROGAEV, et al., "Familial Alzheimer's disease in kindreds with missense mutations in a gene on a chromosome 1 related to the Alzheimer's disease type 3 gene," <i>Nature</i> 376(6463):775-6 (1995)			
	EI	ROTELLO, D.P., "Fencloramine Sulfonamide Inhibition of Amyloid β -Peptide Production by the γ -Secretase Proteolytic Pathway: Potential Small Molecule Therapeutic Agents for the Treatment of Alzheimer's Disease," <i>Chemtracts - Organic Chemistry</i> 13:828-829 (2000)			
	EJ	ROUVINEN, et al., "Computer aided drug design," <i>Acta Pharmaceutica Fennica</i> 97, 159-166 (1988)			
	EK	RUMBLE, et al., "Amyloid A4 protein and its precursor in Down's syndrome and Alzheimer's disease," <i>N Engl J Med</i> 320(22):1446-52 (1989)			
	EL	SELKOE, et al., "Translating cell biology into therapeutic advances in Alzheimer's disease," <i>Nature</i> 399(6738 Suppl):A23-31 (1999)			
	EM	SHERRINGTON, et al., "Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease," <i>Nature</i> 376(6534):754-60 (1995)			
	EN	SINHA & LIEBERBURG, "Cellular mechanisms of beta-amyloid production and secretion," <i>Proc Natl Acad Sci U S A</i> 96(20):11046-53 (1999)			
	EO	SINHA, et al., "Purification and cloning of amyloid precursor protein beta-secretase from human brain," <i>Nature</i> 402(6761):537-40 (1999)			
	EP	STEINER, et al., "Expression of Alzheimer's disease-associated presenilin-1 is controlled by proteolytic degradation and complex formation," <i>J Biol Chem</i> 273(48):32522-31 (1998)			

Examiner Signature		Date Considered	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT		Complete if Known	
(use as many sheets as necessary)		Application Number	10/820,953
		Filing Date	April 4, 2004
		First Named Inventor	Jordan J.N. Tang
		Art Unit	Not Yet Assigned
		Examiner Name	Not Yet Assigned
Sheet	10	of	11
		Attorney Docket Number	022266-000940US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
	EQ	SUZUKI, et al., "An increased percentage of long amyloid beta protein secreted by familial amyloid beta protein precursor (beta APP717) mutants," <i>Science</i> 264(5163):1336-40	
	ER	SYMERSKY, et al., "High-resolution structure of the extracellular eucropic protease from <i>Candida tropicalis</i> yeast," <i>Biochemistry</i> 36(42):12700-10 (1997)	
	ES	SZOSTAK, "In vitro genetics," <i>TIBS</i> 18:69 (1992)	
	ET	TAGAWA, et al., "Alzheimer's disease amyloid beta-clipping enzyme (APP secretase) identification, purification, and characterization of the enzyme," <i>Biochemical and Biophysical Research Communications</i> 177(1):377-387 (1991).	
	EU	TAKAHASHI, <i>Aspartic Proteases, Structure, Function, Biology, Biomedical Implications</i> , <i>Adv. in Exptl. Med. Biol.</i> 382 (Plenum Press, NY 1995).	
	EV	TANG, <i>Acid Proteases, Structure, Function and Biology</i> , <i>Adv. in Exptl. Med. Biol.</i> vol. 95 (Plenum Press, NY 1977).	
	EW	TANG, et al., "Structural evidence for gene duplication in the evolution of the acid es," <i>Nature</i> 271(5646):616-21 (1978)	
	EX	TANZI, et al., "Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease," <i>Nature</i> 331(6156):528-30 (1988).	
	EY	The early story of Alzheimer's Disease, edited by Bick et al. (Raven Press, New York 1987).	
	EZ	THINAKARAN, et al., "Endoproteolysis of presenilin 1 and accumulation of processed derivatives in vivo," <i>Neuron</i> 17(1):181-90 (1996).	
	FA	THINAKARAN, et al., "Evidence that levels of presenilins (PS1 and PS2) are coordinately regulated by competition for limiting cellular factors," <i>J Biol Chem</i> 272(45):28415-22 (1997).	
	FB	THINAKARAN, et al., "Stable association of presenilin derivatives and absence of presenilin interactions with APP," <i>Neurobiol Dis</i> 4(6):438-53 (1998)	
	FC	TURNER et al., "Substrate specificity of memapsin 2 (B-secretase): basis for inhibitor drug designed for Alzheimer's disease," <i>Experimental Biology 2001</i> (re: FASEB Office of Scientific March 31-April 4, 2001, Orlando, Florida. (Abstract)	
	FD	VAN BREEKHoven, et al., "Amyloid beta protein precursor gene and hereditary cerebral hemorrhage with amyloidosis (Dutch)," <i>Science</i> 248(4959):1120-2 (1990).	
	FE	VARON, S., et al., "Neurotrophic and Neurite-Promoting Factors and Their Clinical Potentials", <i>Dev. Neurosci</i> (1983)14: 673-100	'
	FF	VASSAR, et al., "Beta-secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE," <i>Science</i> 286(5449):736-41 (1999).	

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				Art Unit	Not Yet Assigned
				Examiner Name	Not Yet Assigned
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	FG	WOLFE, et al., "Two transmembrane aspartates in presenilin-1 required for presenilin endoproteolysis and gamma-secretase activity," <i>Nature</i> 398(6727):513-7 (1999).		T ²
	FH	YANG & QUAJL, "Structure of the Rhizomucor miehei aspartic proteinase complexed with inhibitor pepstatin A at 2.7 A resolution," <i>Acta Crystallogr D Biol Crystalogr</i> 55 (Pt 3):328-30 (1999)		
	FI	YOSHIKAI, et al., "Genomic organization of the human amyloid beta-protein precursor gene," <i>Gene</i> 87(2):257-63 (1990).		
	FJ	YU, "Inhibition of beta-amyloid cytotoxicity by midline," <i>Neurosci Lett</i> 254(3):125-8 (1998).		
	FK	Database Swissprot, Database Accession No. P28712, December 1, 1992		
	FL	Database Swissprot, Database Accession No. P56272, July 15, 1998		

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